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Subject: Environmental Defense comments on Methyl Acetoacetate (CAS# 105-45-3)

(Submitted via Internet 6/22/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and Jlr@cpma.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Methyl Acetoacetate (CAS# 105-45-3).

The test plan and robust summaries for methyl acetoacetate (MAA) were submitted by The Color Pigments Manufacturing Association. The submission is clearly written and the data are presented in an objective manner. According to the test plan, the primary use of MAA is in the production of color pigments. Secondary uses are not identified, although the sponsor states that MAA is used and transported in closed systems and worker, environmental and consumer exposures are unlikely. However, the sponsor does not propose a reduced testing requirement because of the claim that MAA is handled and transported in closed systems. No monitoring data are provided in the test plan or robust summaries.

Existing data found in the test plan and robust summaries address all SIDS endpoints, so the sponsor does not propose additional tests. We agree with the sponsor that the existing data are adequate to meet HPV requirements and that MAA appears to possess low toxicity for ecological and mammalian systems. Nevertheless, we do have some methodological questions on a couple of the studies presented in the robust summaries, and we also have a few specific comments as indicated below:

1. MAA is readily biodegradable and it appears to be converted to acetoacetic acid in biological systems. We note that MAA has low acute toxicity to fish and aquatic invertebrates but that toxicity is somewhat higher for algae. Is this because of the conversion to acetoacetic acid and subsequent changes in pH of the test system?

2. MAA is negative in the Ames test with or without metabolic activation. In contrast, positive results were observed in Chinese Hamster lung cells for chromosomal aberrations. The sponsor claims that the positive result may have been caused by a lowering of pH. The pH was not monitored in the study presented in the robust summaries, so we suggest that the sponsor replicate this study including pH measurements at appropriate times.

3. Repeat dose studies, including a combined repeat dose/reproductive/developmental toxicity study, indicate that MAA has a low order of toxicity to rodent test systems, with an apparent NOEL of greater than 1 g/kg/day. However, the robust summaries did not state which tissues were subjected to histological analyses. Since the study was conducted according to the OECD 422 guidelines, we expect that the full range of histological analyses were included. Nevertheless, the histological methodologies and results should be summarized in the robust summaries.

Thank you for this opportunity to comment.

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